MPIL 100

Biotechnology and Law. MPIL Research Projects on the Legal Implications of Whole Genome Sequencing

Panna Darazs

Photo: Creative Commons

Biotechnology law, which involves numerous issues of public law and international law, is still a relatively young branch in the 100-year history of the Max Planck Institute for Comparative Public Law and International Law (MPIL) in Heidelberg. The first research projects and actors in this field have only emerged in the 2000s and remained an exceptional phenomenon in the Institute's research agendas. It is remarkable that the field of New Technologies has been able to develop alongside the traditional topics of international law. This article presents the three largest, highly interdisciplinary projects in the field of biotechnology law (also) based at the MPIL. They took place consecutively and partly build on each other. The overarching topics were the legal handling of whole genome sequencing and the question of adequate patient protection from a medicolegal and data protection law perspective.

MPIL 100

I. Research projects

EURAT

In March 2011, the interdisciplinary project *Ethische und Rechtliche Aspekte der Totalsequenzierung des menschlichen Genoms* ("Ethical and Legal Aspects of Whole Genome Sequencing", EURAT) was launched as part of the Marsilius-Kolleg at the Ruprecht Karl University of Heidelberg. Rüdiger Wolfrum and Fruzsina Molnár-Gábor, then a research fellow at the MPIL, and other scientists from the University of Heidelberg, the Heidelberg University Hospital, the *Deutsches Krebsforschungszentrum* (German Cancer Research Center, DKFZ), the European Molecular Biology Laboratory (EMBL) and the Leibniz University Hanover worked on the ethical, legal and economic aspects of whole genome sequencing in clinical applications.

Modern computer-based technologies for analysing human DNA had been developed to such an extent that entire genomes, i.e. the entire genetic information of individual persons, could now be deciphered and analysed in just a few days. Since then, such technologies have been increasingly used in basic research, but also in clinical practice, in order to detect genetically influenced diseases such as certain types of tumours but also certain heart muscle and metabolic diseases, at an early stage and to be able to design patient-specific and personalised prevention and therapy approaches (EURAT Position Paper, 4-5, 37). Storing the data obtained from a genome analysis also makes it possible to make the relevance and function of individual genes the subject of longer-term study (EURAT Position Paper, 64).

From a legal perspective, it was particularly important to analyse the requirements and prerequisites necessary for patient consent. In contrast to conventional medical interventions, where patient consent relates to the consequences and risks of a one-off, singular physical intervention, whole genome sequencing represents an ongoing interference with the rights of the person concerned. The focus is therefore not on the minor physical burden of a blood sample required for genetic analysis. Rather, the successive acquisition of information associated with the sequencing constitutes the actual interference, the scope and extent of which the patient may find difficult to assess at the time of the analysis and therefore might not be able to consent to (EURAT Position Paper, 64-65). Therefore, the current concepts of patient information and patient consent do not appear to do justice to the nature of whole genome sequencing, so that the EURAT Group proposes the expansion of human genetic counselling in the form of a multi-tiered information procedure (EURAT Position Paper, 65).

In the course of a genome-wide analysis, in addition to the intended findings, incidental or additional findings are often made. Although the latter are outside the actual diagnostic objective, they are often medically significant for the person affected. The disclosure of additional findings can have a severe psychological impact on the patient or their relatives and present them with a new life situation (EURAT Position Paper, 66). The research group has

established that scientists have a due diligence duty to report relevant findings as well as additional findings to the attending physician, provided that this is not precluded by the patient's declaration of consent. This also entails that the reporting of additional findings should be covered by and decided on in the declaration of consent on the basis of the patient information provided by the doctor. However, the patient's right not to know must also be taken into account here (EURAT Position Paper, 27, 66-67).

It was also necessary to clarify how the extracted genetic data, which is highly sensitive, can be adequately protected and for what purposes it may be used. This is of great importance not least because whole genome sequencing relies heavily on a division of labour between different, often international, institutes and databases from the clinical and research sectors (EURAT Position Paper, 23, 73).[1] In response to this, the EURAT Group offers, among other things, the ground rule of encoding patient data. Thereby, all sequence data must be stored pseudonymised (EURAT Position Paper, 15, 72, 82). Passing on the code for decryption or the decrypted data must be prohibited. The rules for using the data should further be based on the provisions of the applicable data protection laws (EURAT Position Paper, 15, 73, 80-81).[2]

In June 2013, the EURAT Group published its research findings and the subsequent practical suggestions for dealing with the new possibilities of biomedical technology in the form of a position paper (EURAT Position Paper, 5). In addition to a code of ethical principles and legal guidelines for carrying out genome analyses addressed to non-physicians involved in genome sequencing, the statement contains two sample texts for patient information and consent forms for the purposes of diseases identification and cancer research (EURAT Position Paper, 6, 12-20, 32-56). The main idea is to strengthen responsible and fiduciary behaviour of those involved in genome sequencing, both in basic research and in the practical application of patient care. The aim is not to promote regulation by the state, but rather to foster the ability of scientists and medical practitioners to self-regulate their actions (EURAT Position Paper, 6). The principles and guidelines developed are therefore intended to be binding also for non-medical scientists. In addition, the respective research institutes are encouraged to incorporate the code into their

[1] Compare: Art. 9 para. 1 GDPR; "Eckpunkte für eine Heidelberger Praxis der Ganzgenomsequenzierung", Heidelberg 2013 (EURAT Position Paper); The position paper was also published in an updated 2nd edition in 2015.

[2] The points of reference for data protection regulation, as developed by the group, in detail: EURAT Position Paper, 74-86.

internal provisions and allow their scientists to participate in regular training (EURAT Position Paper, 18).

The aim of the EURAT research group was to contribute its findings to policy advice and the development of statements to be considered in German legislative procedures, but also to contribute to international discussions. With its position paper, the project also aimed to establish a nationally and internationally accessible platform in Heidelberg for the discussion of normative questions of genome analysis across disciplines and thereby the promotion of international scientific exchange.[3]

Collaborative Research Project of the Ministry of Education and Research

The findings of the EURAT Group were further developed in a collaborative research project funded by the German Federal Ministry of Education and Research (*Bundesministerium für Bildung und Forschung*, BMBF) between 2013 and 2015 and in 2016 published in a report titled *Genomanalysen als Informationseingriff. Ethische, juristische und ökonomische Analysen zum prädiktiven Potential der Genomsequenzierung* ("Genome analyses as an information intervention. Ethical, legal and economic analyses on the predictive potential of genome sequencing") in the Marsilius-Kolleg publication series.[4] The project was divided into three sub-areas, analysing the implementation of genome sequencing for predictive purposes from the perspective of ethics, law, and health economy. Numerous experts from the DKFZ and the Heidelberg University Hospital, as well as the Max Planck Institute for Molecular Genetics and the entire EURAT-group from Heidelberg were involved in the implementation of this research project.[5] The legal sub-project was led by Rüdiger Wolfrum and Fruzsina Molnár-Gábor (MPIL) and by Paul Kirchhof (Heidelberg University).[6] The legal and ethics sub-projects were based in Heidelberg, while the health economics part was housed at the University of Hanover.[7] The aim of the interdisciplinary project was to develop a "good clinical practice" of whole genome sequencing with regard to its predictive potential while at the same time preserving the integrity of the patient.[8]

The boundary between "healthy" and "ill" is ambiguous in the field of predictive genetic tests, so that the attribution of a certain risk of disease can push the patient or the person seeking advice into the role of someone who is no longer healthy but only pre-symptomatic.[9] For this

[3] MPIL, Ethische und rechtliche Aspekte der Totalsequenzierung des menschlichen Genoms, Über das Projekt.
[4] *Klaus Tanner et al, Genome analyses as information intervention. Ethical, legal and economic aspects* Analyses of the predictive potential of genome sequencing, Schriften des Marsilius Kollegs, vol. 15, Heidelberg: Universitätsverlag Winter 2016.
[5] *Tanner et al.* (fn. 5), 10.
[6] *Tanner et al.* (fn. 5), 11.
[7] University of Heidelberg, BMBF Verbundprojekt.
[8] *Tanner et al.* (fn. 5), 9.
[9] *Tanner et al.* (fn. 5), 13.

reason, it was discussed whether an extension of the definitory scheme of diagnoses would be useful. Such an extension would include a term which "captures the, with a certain degree of probability, future occurrence of a diagnosis"[10]. The use of the term *Prädiktionsdiagnose* ("predictive diagnosis") was proposed for additional findings. This wording refers to a disease that has an increased probability of occurring over the course of a person's life, but at the same does not categorize the person affected as already subjected to the disease.[11]

In a slight departure from the EURAT project, the focus of legal research in this project was placed less on data protection but on the aspects of patient consent, patient information and the rights and obligations of doctors in the area of additional findings. Data protection aspects are covered rather sparsely and mainly in the last chapter "Outlook and Open Questions".[12] With regard to the significance and handling of additional findings, research results already presented by the EURAT Group were recorded in more detail and in a more multi-faceted manner. For example, different options regarding the reporting of additional findings are discussed in detail, covering a wide range of possibilities: from not reporting findings at all[13], to reporting certain findings guided by positive-[14] or negative lists[15] or the doctor's prerogative[16], or reporting all additional findings without exception[17]. These alternative courses of action are, like other aspects of the publication, analysed not only from a legal, but also from an ethical and economic perspective. In this way, research was carried out into how appropriate patient protection can be ensured through newly developed forms of patient information, patient consent and patient counselling.[18]

"International Biotechnology Governance, exemplified by the Handling of New Genetic Analyses"

In the context of the EURAT research group and the Collaborative Research Project, Fruzsina Molnár-Gábor wrote her dissertation on "International Biotechnology Governance, exemplified by the Handling of New Genetic Analyses" ("*Die internationale Steuerung der Biotechnologie am Beispiel des Umgangs mit neuen genetischen Analysen"*)[19] at the MPIL from 2010 to 2015. It was defended at the Faculty of Law of Heidelberg University and

---

[10] *Tanner et al*. (fn. 5), 14, translated by the editor.
[11] *Tanner et al*. (fn. 5), 14.
[12] *Tanner et al*. (fn. 5), 234-237, translated by the editor.
[13] *Tanner et al*. (fn. 5), 172-173.
[14] *Tanner et al*. (fn. 5), 174-180.
[15] T*anner et al*. (fn. 5), 180-182.
[16] *Tanner et al*. (fn. 5), 182-184.
[17] *Tanner et al*. (fn. 5), 173-174.
[18] MPIL, BMBF Verbundprojekt, Über das Projekt.
[19] *Fruzsina Molnár-Gábor*, Die internationale Steuerung der Biotechnologie am Beispiel des Umgangs mit neuen genetischen Analysen, Ethik und Recht vol. 2, Berlin: Duncker & Humblot 2017, title translated by the editor.

supervised by Silja Vöneky and Rüdiger Wolfrum.[20] The thesis examines the international handling of the normative challenges caused by modern developments in biotechnology, using the example of new genetic analyses, in particular whole genome sequencing. The aim of Fruzsina Molnár-Gábor's research was to describe and uphold the position of the patient as a person. While the first part of the dissertation deals with the status of the person in the development of intellectual history and the international legal system, the second part presents whole genome sequencing as a new diagnostic method. This includes not only a technical description of genome sequencing, but also an explanation and assessment of the challenges associated with its application in research and practice as part of a normative analysis.[21] Finally, in the context of this analysis, the third part discusses the existing and future international governance of whole genome analysis. The focus here is on examining the work of the United Nations Educational, Scientific and Cultural Organisation (UNESCO), which is considered the most important international organisation in the governance of biomedicine. The author impressively demonstrates "what influence the consideration of the characteristics and challenges of whole genome analysis in the governance of genetic analyses has had, *de lege lata*, on the factors of its recognition and, *de lege ferenda*, can have".[22]

II. Conclusion

The projects described above mark the emergence of a new area of research at the MPIL. This area of activity, which was established at the Institute during Rüdiger Wolfrum's directorship, may have remained peripheral. However, its growing topicality, future-oriented nature and the associated new demands for legal regulation call for recognition of the results and the researchers involved in these projects on the occasion of the 100th anniversary of the MPIL. The issues of biotechnology law taken up in the early 2000s remain closely intertwined with the basic research conducted at the Institute on human dignity, the right to self-determination, the right to know and the right not to know. The deciphering of DNA generates highly sensitive personal data, the medical utilisation of which is essential for the development of new therapeutic approaches, but also entails the risk of misuse and thus violations of personal rights. Particularly in view of the globalized research in the field of biotechnology and the potential uses of genetic data, it is important that new regulations are created in this field to safeguard the fundamental rights concerned. This is also why a future transnational legal harmonisation of biotechnology law – at least at the European level – seems necessary. The scientific patronage of this process is a new and challenging task that could again be linked more closely to the current research of the MPIL.

---

[20] *Molnár-Gábor* (fn. 20), 7.
[21] *Molnár-Gábor* (fn. 20), 19.
[22] *Molnár-Gábor* (fn. 20), 20-21; University of Heidelberg, Zusammenfassung der Dissertation mit dem Titel „Die internationale Steuerung der Biotechnologie am Beispiel des Umgangs mit neuen genetischen Analysen", 11.

MPIL 100

Translation from the German original: Sarah Gebel.